

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

BIRD GOEN & CO.
Vilvoordsebaan 92
B-3020 Winksele
BELGIQUE

Date of mailing (day/month/year) 06 November 2001 (06.11.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference D 1313 PCT	
International application No. PCT/EP00/06345	International filing date (day/month/year) 05 July 2000 (05.07.00)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input type="checkbox"/> the inventor	<input type="checkbox"/> the agent <input type="checkbox"/> the common representative
Name and Address ROCHE DIAGNOSTICS GMBH Sandhofer Strasse 116 D-68305 Mannheim Germany	State of Nationality DE	State of Residence DE
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input checked="" type="checkbox"/> the person	<input checked="" type="checkbox"/> the name	<input checked="" type="checkbox"/> the address <input checked="" type="checkbox"/> the nationality <input checked="" type="checkbox"/> the residence
Name and Address K.U. LEUVEN Groot Begijnhof 59 B-3000 Leuven Belgium	State of Nationality BE	State of Residence BE
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Gabriele BAEHR Telephone No.: (41-22) 338.83.38
---	--

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 01 March 2001 (01.03.01)	Applicant's or agent's file reference D 1313 PCT
International application No. PCT/EP00/06345	Priority date (day/month/year) 05 July 1999 (05.07.99)
International filing date (day/month/year) 05 July 2000 (05.07.00)	
Applicant CAUWENBERGHS, Nancy et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

05 January 2001 (05.01.01)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

F. Baechler

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

To:

BIRD GOEN & CO.
Vilvoordsebaan 92
B-3020 Winksele
BELGIQUE

Date of mailing (day/month/year) 13 December 2001 (13.12.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference D 1313 PCT	
International application No. PCT/EP00/06345	International filing date (day/month/year) 05 July 2000 (05.07.00)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input type="checkbox"/> the inventor	<input type="checkbox"/> the agent <input type="checkbox"/> the common representative
Name and Address K.U. LEUVEN Groot Begijnhof 59 B-3000 Leuven Belgium	State of Nationality BE	State of Residence BE
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input type="checkbox"/> the person	<input checked="" type="checkbox"/> the name	<input type="checkbox"/> the address <input type="checkbox"/> the nationality <input type="checkbox"/> the residence
Name and Address K.U. LEUVEN RESEARCH & DEVELOPMENT Groot Begijnhof 59 B-3000 Leuven Belgium	State of Nationality BE	State of Residence BE
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Gabriele BAEHR
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

10575
(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
11 January 2001 (11.01.2001)

PCT

(10) International Publication Number
WO 01/02853 A2

(51) International Patent Classification⁷: G01N 33/48

(21) International Application Number: PCT/EP00/06345

(22) International Filing Date: 5 July 2000 (05.07.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
99112967.7 5 July 1999 (05.07.1999) EP

(71) Applicant (for all designated States except US): ROCHE
DIAGNOSTICS GMBH [DE/DE]; Sandhofer Strasse
116, D-68305 Mannheim (DE).

B-9032 Gent (BE). VANHOORELBEKE, Karen
[BE/BE]; Ommegangstraat 3, B-8550 Zwevegem (BE).
DECKMYN, Hans [BE/BE]; Lemingstraat 1, B-3210
Linden (BE).

(74) Agent: VOSSIUS & PARTNER; Siebertstr. 4, D-81675
München (DE).

(81) Designated States (national): JP, US.

(84) Designated States (regional): European patent (AT, BE,
CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,
NL, PT, SE).

Published:

— Without international search report and to be republished
upon receipt of that report.

(72) Inventors; and

(75) Inventors/Applicants (for US only): CAUWEN-
BERGHS, Nancy [BE/BE]; Benningsbrugstraat 56A,

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: DETECTION OF VON-WILLEBRAND FACTOR (vWF) ACTIVITY

(57) Abstract: The present invention relates to a method for detecting von-Willebrand factor (vWF) activity comprising assaying a sample in the presence of a soluble form or portion of glycoprotein Ib(α) (GPIb(α)) and ristocetin, or a functionally equivalent substance. Additionally, the invention relates to the use of the aforementioned soluble form or portion of glycoprotein Ib(α), of ristocetin or a functional equivalent substance, of specifically reacting anti-GPIb(α) antibody(ies) and/or of specific binding partners, like specifically reacting anti-vWF antibody(ies) for carrying out the method of the invention. Furthermore, the present invention relates to kits for carrying out the method of the invention.

WO 01/02853 A2

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 00/06345

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/86

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	VANHOORELBEKE KAREN ET AL: "A reliable and reproducible ELISA method to measure ristocetin cofactor activity of von Willebrand factor." THROMBOSIS AND HAEMOSTASIS, vol. 83, no. 1, January 2000 (2000-01), pages 107-113, XP000974940 ISSN: 0340-6245 the whole document	1-30
X	WO 92 16225 A (BRIGHAM & WOMENS HOSPITAL) 1 October 1992 (1992-10-01) page 38, paragraph 3 page 39, line 5,6 claim 17	1-30
	--- -/-	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- * & * document member of the same patent family

Date of the actual completion of the international search

3 January 2001

Date of mailing of the international search report

25/01/2001

Name and mailing address of the ISA

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NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Pellegrini, P

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 00/06345

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HOYLAERTS MARC F ET AL: "Promotion of binding of von Willebrand factor to platelet glycoprotein Ib by dimers of ristocetin." BIOCHEMICAL JOURNAL, vol. 306, no. 2, 1995, pages 453-463, XP000974675 ISSN: 0264-6021 cited in the application page 457, column 2, paragraph 3 -page 458, column 2, paragraph 1 -----	1-30
A	US 5 231 033 A (FICKENSCHER KARL) 27 July 1993 (1993-07-27) the whole document -----	1-30

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 00/06345

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9216225	A	01-10-1992	US	5321127 A	14-06-1994
			AU	1655092 A	21-10-1992
US 5231033	A	27-07-1993	DE	4016885 A	28-11-1991
			AT	135109 T	15-03-1996
			AU	655415 B	22-12-1994
			AU	7621591 A	28-11-1991
			CA	2043214 A	26-11-1991
			DE	59107497 D	11-04-1996
			EP	0458330 A	27-11-1991
			ES	2085926 T	16-06-1996
			JP	3018588 B	13-03-2000
			JP	4231871 A	20-08-1992

PATENT COOPERATION TREATY

PCT



REC'D 17 OCT 2001

WIPO

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference D 1313 PCT		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)			
International application No. PCT/EP00/06345	International filing date (day/month/year) 05/07/2000	Priority date (day/month/year) 05/07/1999			
International Patent Classification (IPC) or national classification and IPC G01N33/48					
Applicant [ROCHE DIAGNOSTICS GMBH et al.] K.U. LEUVEN					
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>					
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none">I <input checked="" type="checkbox"/> Basis of the reportII <input type="checkbox"/> PriorityIII <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicabilityIV <input type="checkbox"/> Lack of unity of inventionV <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statementVI <input type="checkbox"/> Certain documents citedVII <input checked="" type="checkbox"/> Certain defects in the international applicationVIII <input checked="" type="checkbox"/> Certain observations on the international application					
Date of submission of the demand 05/01/2001		Date of completion of this report 12.10.2001			
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Weijland, A Telephone No. +49 89 2399 7490 			

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/06345

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-28 as originally filed

Claims, No.:

1-30 as originally filed

Drawings, sheets:

1/9-9/9 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/06345

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	4,6,12,14,18,19,28,29
	No:	Claims	1-3,5,7-11,13,15-17,20-22,24-27,30
Inventive step (IS)	Yes:	Claims	23
	No:	Claims	1-22,24-30
Industrial applicability (IA)	Yes:	Claims	1-30
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

The following documents (D) are referred to in this report; the numbering will be adhered to the rest of the procedure:

- D1: VANHOORELBEKE KAREN ET AL: 'A reliable and reproducible ELISA method to measure ristocetin cofactor activity of von Willebrand factor.' THROMBOSIS AND HAEMOSTASIS, vol. 83, no. 1, January 2000 (2000-01), pages 107-113, XP000974940 ISSN: 0340-6245
- D2: WO 92 16225 A (BRIGHAM & WOMENS HOSPITAL) 1 October 1992 (1992-10-01)
- D3: HOYLAERTS MARC F ET AL: 'Promotion of binding of von Willebrand factor to platelet glycoprotein Ib by dimers of ristocetin.' BIOCHEMICAL JOURNAL, vol. 306, no. 2, 1995, pages 453-463, XP000974675 ISSN: 0264-6021 cited in the application

SECTION V

1. Novelty (Article 33(2) PCT)

1.1 The subject matter of claims 1-3,5,7-11,13,15-17, 20-22,24-27,30 is not novel.

Claims 1-3,5,7-11,13,15,16,20-22,24-27 are anticipated by D3. D3 (abstract; page 454, second and fourth paragraph) describes the interaction between purified vWF and GPIb ("method of detecting von-Willebrand factor activity" or "complex" according to present claims 1, 2,5). GP1b was purified from platelets after solubilization ("soluble" according to present claim 24) over an anti-GP1b antibody ("anti-GPIb antibody" according to present claim 26) coated sepharose column. Purified GPIb ("glycoprotein Ib(α)" according to present claim 1) was coated on wells of microtiter plates ("solid support", "plastic", "microtiter plate", "heterogeneous" according to present claims 3,10,11,13,15) and they were incubated with purified vWF from plasma ("blood sample", diluted" according to present claims 20 to 22) and ristocetin ("ristocetin" according to present claims 1 and 25). GPIb associated vWF was revealed by horse radish peroxidase conjugated anti-vWF monoclonal antibodies ("anti-vWT antibody" according to present claims 7, 8,9,27) in an ELISA assay ("ELISA" according to present claim 16).

Claims 1, 17 and 30 are anticipated by D2. D2 (abstract; page 42, second paragraph) describes recombinant Gplb(α) in an agglutination assay comprising a recombinant Gplb(α) polypeptide ("GP1b(α) is recombinantly produced" according to present claim 30) and vWF.

1.2 Claims 4,6,12,14,18,19,23, 28,29 are novel, since they are not disclosed in the prior art documents.

2. Inventive Step (Article 33(3) PCT).

2.1 Dependent claims 4, 6,12,14,18,19 do not contain any features which, in combination with the features of claim 1 to which they refer, meet the requirements of the PCT in respect of inventive step, since these features can be considered as mere alternatives for the skilled person in the art, without that they add to claim 1 any unexpected effect whatsoever.

2.2 Claims 28 and 29, relating to a kit or the use thereof comprising the components (a) to (d), do not involve an inventive step, since it would be obvious for the skilled person to bring together in the form of a kit, the components needed to carry out a non-inventive method. A kit for a non-inventive method itself is thus not inventive.

2.3 Claim 23 would appear to involve an inventive step.

D3 (see section 1.1 above) is considered to be the closest prior art. Claim 23 differs from D3 in that it relates to a method for discrimination between von Willebrand disease typ I and II in that it determines the total amount of vWF antigen and the vWF activity in a test sample.

The technical problem to be solved would reside in further applications of the vWF activity assay to overcome problems known in the prior art accompanied with these assays (see pages 2 to 4 of the description).

The skilled person, equipped with the knowledge of D3, would not be motivated to arrive at the subject matter of claim 23, since it has not been suggested in D3 alone or in combination with any other prior art document, that discrimination

between vWF type I and vWF type II can be accomplished by steps (a) to (d) and moreover that means are thus provided for a more reproducible and more precise test with low inter and intra-assay variability (see page 5, second paragraph of the description).

3. The priority date of the present application, i.e. 05.07.1999, is validly claimed and therefore D1 does not form part of the state of the art.

SECTION VII

4. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in D2 is not mentioned in the description, nor are these documents identified therein.

SECTION VIII

5. The passage "or a functional equivalent substance" renders the subject matter of claim 1 for which protection is sought unclear and contravenes Article 6 PCT.
6. The use of optionally features in the passage "optionally further comprising...." renders the subject matter that follows this passage non limiting for the scope of claim 29 and introduces ambiguity in said scope and so contravenes Article 6 PCT.

PATENT COOPERATION TREA

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference D 1313 PCT	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 00/06345	International filing date (day/month/year) 05/07/2000	(Earliest) Priority Date (day/month/year) 05/07/1999
Applicant ROCHE DIAGNOSTICS GMBH et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

DETECTION OF VON-WILLEBRANDFACTOR (VWF) ACTIVITY

5. With regard to the **abstract**,

the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.

1



None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 00/06345

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/86

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	VANHOORELBEKE KAREN ET AL: "A reliable and reproducible ELISA method to measure ristocetin cofactor activity of von Willebrand factor." THROMBOSIS AND HAEMOSTASIS, vol. 83, no. 1, January 2000 (2000-01), pages 107-113, XP000974940 ISSN: 0340-6245 the whole document	1-30
X	WO 92 16225 A (BRIGHAM & WOMENS HOSPITAL) 1 October 1992 (1992-10-01) page 38, paragraph 3 page 39, line 5,6 claim 17	1-30

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- * & * document member of the same patent family

Date of the actual completion of the international search

3 January 2001

Date of mailing of the international search report

25/01/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Pellegrini, P

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 00/06345

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HOYLAERTS MARC F ET AL: "Promotion of binding of von Willebrand factor to platelet glycoprotein Ib by dimers of ristocetin." BIOCHEMICAL JOURNAL, vol. 306, no. 2, 1995, pages 453-463, XP000974675 ISSN: 0264-6021 cited in the application page 457, column 2, paragraph 3 -page 458, column 2, paragraph 1 ---	1-30
A	US 5 231 033 A (FICKENSCHER KARL) 27 July 1993 (1993-07-27) the whole document -----	1-30

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 00/06345

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9216225 A	01-10-1992	US 5321127 A AU 1655092 A	14-06-1994 21-10-1992
US 5231033 A	27-07-1993	DE 4016885 A AT 135109 T AU 655415 B AU 7621591 A CA 2043214 A DE 59107497 D EP 0458330 A ES 2085926 T JP 3018588 B JP 4231871 A	28-11-1991 15-03-1996 22-12-1994 28-11-1991 26-11-1991 11-04-1996 27-11-1991 16-06-1996 13-03-2000 20-08-1992